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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/445,865	02/11/00	BURKE	P ERD100

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EXAMINER	
NICKOL,G	
ART UNIT	PAPER NUMBER
1642	17

DATE MAILED: 10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/445,865	Applicant(s) BURKE ET AL.	
	Examiner Gary B. Nickol Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,31-33,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29, 31-33,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

The Amendment filed July 16, 2001 (Paper No. 12) in response to the Office Action of April 10, 2001 is acknowledged and has been entered. Claims 1-28, 30, and 34-39 were cancelled. Claim 41 was added. Claims 29, 31-33, and 40-41 are pending and are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained

Newly amended claims 29, 31-33, and 40 remain rejected and new claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record in Paper No. 9, pages 4-7.

Applicant's argue (Paper No. 12, page 4) that CB 1954 is a proven anti-tumor agent as defined by *in vivo* work in rats, in which CB 1954 is activated by the enzyme NQO1. Applicants further argue that that the present invention incorporates human "NQO2"- by its homology to NQO1 and that it has been shown that human NQO2 can activate CB 1954 in the presence of a specific co-substrate.

These arguments have been considered but are not found persuasive for reasons of record. The claims are broadly drawn to a method of "treating" a human patient with cancer. However, applicants have only assessed the in-vitro cytotoxicity of CB 1954 following transfection of cells with NQO2. And, as mentioned in the previous Action, the greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in- vitro assay does not permit a single extrapolation of in vitro assays to human therapeutic efficacy with any reasonable degree of predictability. Further, applicants assertion that CB 1954 is a proven anti-tumor agent *in vivo* obscures the facts. The specification only teaches (page 6, lines 1-10) that CB 1954 was effective against rat Walker tumors presumably because they contained a high concentration of the enzyme NQO1. However, the human form of NQO1 does not appreciably convert CB 1954 into cytotoxic agent and *human tumors are resistant to this agent.*

Applicants further argue that that the actual compound responsible for the cytotoxic effect is the same as that shown to elicit the same effect in response to activation by NQO1 and therefore will function as claimed. This argument has been considered but it not found persuasive. The cytotoxic drug created by the activity of NQO2 may be the same as that created by NQO1; however, there is no guidance or evidence to suggest that it will function as claimed following the *in vivo* administration of NRH or an analogue thereof in combination with CB 1954 to treat a human patient with cancer. Indeed, by applicants own admission, the examples provided in the disclosure were used to illustrate that the administration of co-substrates *in vitro* is achievable and that their desired effects on the reactions to produce toxicity *in vitro* were obtainable (Paper No. 12, page 5). Applicants further concede that they have not extrapolated

the efficacy of the resultant cytotoxic compound from *in vitro* studies. Thus, applicants arguments have not been found persuasive, and the rejection is maintained for reasons of record.

All other objections and or rejections are withdrawn in view of applicant's amendments there to.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol Ph.D.
Examiner
Art Unit 1642

GBN
September 28, 2001

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600